IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Reissue Application	:	Not yet assigned
Serial No.	:	Not yet assigned
Filed	:	January 15, 1999
Patent	:	5,639,940
Patentee	:	Ian Garner, Michael A.. Dalrymple,* Donna E. Prunkard and Donald C. Foster
Assignee	:	Pharmaceutical Proteins, Ltd., and ZymoGenetics, Inc.
Issued	:	June 17, 1997
Application	:	08/206,176
Filed	:	March 3, 1994
For	:	PRODUCTION OF FIBRINOGEN IN TRANSGENIC ANIMALS

REISSUE DECLARATION AND POWER OF ATTORNEY

We, DONNA E. PRUNKARD and DONALD C. FOSTER, two of the four named inventors of United States patent 5,639,940 ("the '940 patent"), and applicants for reissue thereof, declare that:

1. We are citizens of the United States and have residences and post office addresses as stated below under our respective names:

Donna E. Prunkard
1463 N.W. 92nd St.
Seattle, WA 98117

* The '940 patent incorrectly printed the middle initial of Dr. Dalrymple as "L".

EXPRESS MAIL
EI187448225US

Donald C. Foster
3002 NE 181st Street
Lake Forest Park, WA 98155

2. By concurrent Petition Under 37 C.F.R. § 1.324 and Motion Under 37 C.F.R. § 1.634, the four originally named inventors, Ian Garner, Michael A. Dalrymple, Donna E. Prunkard, and Donald C. Foster, have petitioned and moved to correct the inventorship for all of the claims of the '940 patent. As amended, Donna E. Prunkard and Donald C. Foster are the joint inventors of the subject matter claimed in the '940 patent.

3. We have reviewed and understand the contents of the '940 patent and this application for reissue thereof, including their claims, and believe that we are the original, first and joint inventors of the invention described and claimed in the '940 patent to the extent that a reissue application is being sought on that invention.

4. We make this declaration in support of this application for reissue of the '940 patent and acknowledge our duty to disclose to the United States Patent and Trademark Office all information known to us to be material to the patentability of the reissue application and its claims as defined in 37 C.F.R. § 1.56(a).

5. We do not know and do not believe that our invention was ever patented or described in any printed publication in any country before our invention thereof or more than one year prior to the March 3, 1994 filing date of our United States patent application 08/206,176, which issued as the '940 patent, or in public use or on sale in the United States more than one year prior to that filing date.

6. We believe that the '940 patent is "wholly or partly invalid" because of error, without deceptive intent, by reason of our having claimed more than we had a right to claim in view of the prior art. Specifically, all of the claims of the '940 patent recite methods and

transgenic animals employing "DNA" encoding, respectively, each of the Aα, Bβ and γ chains of fibrinogen. To be patentable over the prior art, we believe that these claims should be limited to genomic DNA and thereby exclude cDNA.

7. In obtaining allowance of the claims of the '940 patent, we understand that our attorney argued that the claims were patentable over the prior art based on the unexpected production of useful amounts of biologically active, fibrinogen in the milk of transgenic animals. See Amendment, May 8, 1995, pp. 9-12. We understand that at the request of the Examiner and in view of that argument, our attorney then amended the claims to recite "biocompetent fibrinogen". See Office Action, Paper No. 13, May 21, 1996, p. 4; Amendment, October 1, 1996, pp. 1-2, 6-8. It was this amendment that we understood led to allowance of the claims and grant of the '940 patent.

8. We do not believe that such amendment renders the claims of the '940 patent patentable over the prior art. We believe at the time we made our invention, in view of art published more than one year before the filing date of the application that issued as the '940 patent that it would have been obvious to the skilled worker in the recombinant fibrinogen expression and transgenic arts that biocompetent fibrinogen would be produced in the milk of transgenic animals carrying the cDNAs encoding the Aα, Bβ and γ chains of fibrinogen at about the same level on a per cell basis as had already been produced in mammalian cells transfected with those cDNAs, i.e., about 5μg/mg of cellular protein/day. Indeed, we understood that when such cDNAs were actually used to produce transgenic mice, those mice produced in their milk biocompetent fibrinogen at about that expected level.

9. We also believe that at the time we made our invention, in view of prior art published more than one year before we filed our application, that the skilled worker would

have reasonably expected that genomic DNAs encoding the Aα, Bβ and γ chains of fibrinogen could be used to produce biocompetent fibrinogen in the milk of transgenic animals in the best case at that same level and potentially at much lower levels. We believe, however, that at the time we made our invention, in view of prior art published more than one year before we filed our application, it would not have been obvious to that skilled worker that those genomic DNAs could be used to produce biocompetent fibrinogen in the milk of transgenic animals with a reasonable expectation of success at levels on a per cell basis higher than those already produced in mammalian cells transfected with cDNAs encoding the three fibrinogen claims. It was to this unexpectedly high expression level that we understood our attorney was referring when he argued to the Examiner that our invention was patentable because it unexpectedly produced useful amounts of biocompetent fibrinogen.

10. We believe that the error described in paragraphs 7-9 above arose without deceptive intent. All of the examples in our application used genomic DNA encoding the Aα, Bβ and γ chains of human fibrinogen. We understood that when our attorney made the above arguments to the Examiner and amended our claims to obtain their allowance he had in mind the genomic DNA as used in our Examples. See the '940 patent, Examples II, III, and IV. We understood that he failed to consider that the claims literally included cDNA.

11. We also believe that the '940 patent is also "wholly or partly inoperative" because of error, without deceptive intent, by reason of our having claimed less than we had a right to claim in view of the disclosure of the application that issued as the '940 patent. Specifically, none of the patent claims is directed to a set comprising a first, second, and third DNA segment encoding a secretion signal operably linked to the heterologous fibrinogen Aα, Bβ and γ chains, respectively, each of the DNA segments comprising genomic DNA encoding

the respective fibrinogen chain, and wherein each of the chains is from the same species and is operably linked to additional DNA segments required for expression in the mammary glands of a host female mammal. This set of DNA segments is useful in the methods of claims 1-20 and 23-25 of the '940 patent and in producing the non-human mammals of claims 21-22 and 26-33 of the '940 patent. This set of DNA segments is also described and enabled in the '940 patent and should have been claimed in that patent and in the application from which it issued. Without a claim to this set of DNA segments, we understand that a third party might potentially prepare the recited set of DNA segments in the United States and export that set from the United States for use outside the United States in the production of fibrinogen in the milk of transgenic animals. We also understand that without reissue such acts would not infringe the claims of the '940 patent.

12. We understand and believe that the error described in paragraph 11 arose without deceptive intent.

13. We understand and believe that these errors in the claims of the '940 patent were discovered while reviewing the '940 patent, with counsel, in connection with Garner v. Velander, Interference 104,242. We have filed this reissue application promptly after recognizing the errors.

14. As named inventors, we hereby appoint the following attorneys and agents in connection with the '940 patent and this application for reissue thereof, with full power to prosecute this application for reissue and to transact all business in the United States Patent and Trademark Office in connection therewith and with the '940 patent:

James F. Haley (Reg. No. 27,794)

Karen Mangesarian (Reg. No. p43,772)

Z. Ying Li (Reg. No. 42,800)

all of Fish & Neave, 1251 Avenue of the Americas, 49th Floor, New York, NY 10020

Send correspondence to: James F. Haley, Jr.
1251 Avenue of the Americas
New York, New York 10020-1104

Direct telephone calls to: James F. Haley
(212) 596-9000

15. We hereby declare that we understand the English language, and that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application for reissue or any Patent issued thereon.

Donna E Prunkard
DONNA E. PRUNKARD

Date: 1-13-99

DONALD C. FOSTER

Date: 1-13-99

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Filed	:	January 15, 1999
Patent	:	5,639,940
Patentee	:	Ian Garner, Michael A. Dalrymple,* Donna E. Prunkard and Donald C. Foster
Assignee	:	Pharmaceutical Proteins, Ltd., and ZymoGenetics, Inc.
Issued	:	June 17, 1997
Application	:	08/206,176
Filed	:	March 3, 1994
For	:	PRODUCTION OF FIBRINOGEN IN TRANSGENIC ANIMALS

DECLARATION IN SUPPORT OF REISSUE APPLICATION

I, GARY E. PARKER, declare that:

1. I make this declaration in support of the accompanying Reissue Application for United States patent 5,639,940.

2. I am Principle Patent Agent at ZymoGenetics, Inc., Seattle, Washington. In March 1994, I was the Manager of the Patent Department at ZymoGenetics. I am registered to practice before the United States Patent and Trademark Office. I am not an attorney.

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* The '940 patent incorrectly printed the middle initial of Dr. Dalrymple as "L".

3. I prepared and filed the '176 application that issued as the above-identified '940 patent.

4. I understand and believe that the '940 patent is "wholly or partly invalid" because of error, without deceptive intent. I believe that the patent claims more than the inventors had a right to claim in view of the prior art. Particularly, all of the claims of the '940 patent recite methods and transgenic animals employing "DNA" encoding, respectively, each of the Aα, Bβ and γ chains of fibrinogen. I believe that these claims should be limited to genomic DNA, and thereby exclude cDNA, to be patentable over the prior art.

5. In obtaining allowance of the claims of the '940 patent over the prior art, I argued that the claims were patentable because production of useful amounts of biologically active, fibrinogen in the milk of transgenic animals was unexpected. See Amendment, May 8, 1995, pp. 9-12. At the request of the Examiner and in view of that argument, I amended the claims to recite "biocompetent fibrinogen". See Office Action, Paper No. 13, May 21, 1996, p. 4; Amendment, October 1, 1996, pp. 1-2, 6-8. I believe that it was this amendment that led to allowance of the claims and grant of the '940 patent.

6. I do not now believe that my amendment renders the claims of the '940 patent patentable. I understand and believe that at the time the inventors made their invention in view of art published more than one year before the filing date of the application that issued as the '940 patent, it would have been obvious to the skilled worker in the recombinant fibrinogen expression and transgenic arts that biocompetent

human fibrinogen would be produced in the milk of transgenic animals carrying the cDNAs encoding the Aα, Bβ and γ chains of human fibrinogen at about the same level on a per cell basis as had already been produced in mammalian cells transfected with those cDNAs, i.e., about 2μg/2x10^{6}cells/day.* In fact, when cDNAs encoding the three chains of fibrinogen were used to produce transgenic mice, those mice produced biocompetent fibrinogen in their milk at about the expected level.

7. I also understand and believe that at the time of invention, in view of prior art published more than one year before the application was filed, that it would not have been obvious to that skilled worker that genomic DNAs encoding the Aα, Bβ and γ chains of fibrinogen could be successfully used to produce biocompetent fibrinogen in the milk of transgenic animals at levels on a per cell basis higher than those already produced in mammalian cells using the corresponding cDNAs. It was to this unexpectedly higher production of biocompetent fibrinogen which I referred when I argued that the Garner claims were patentable. *See, supra*, ¶ 5.

8. I believe that the error described in paragraphs 4-7 above arose without deceptive intent. Although I do not recall the specific details of the prosecution of the application that issued as the '940 patent, I believe that during prosecution I did not consider that the claims covered low level expression of cDNA. All of the examples in the application used genomic DNA encoding the Aα, Bβ and γ chains of human fibrinogen. See the '940 patent, Examples II, III, and IV. And, it was only genomic DNA that the inventors had used to produce useful amounts of biocompetent fibrinogen in the milk of

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* During prosecution of the application that issued as the Garner '940 patent, the Examiner cited Roy et al. for its report of the production of 2μg of fibrinogen per 2x10^{6}cells/day in COS cells.

transgenic animals. It was this work that was the basis of my patentability arguments. As best I can recollect, I failed to consider or realize that the pending claims literally included cDNA.

9. I also understand and believe that the '940 patent is also "wholly or partly inoperative" because of error, without deceptive intent. I believe that the patent claims less than the inventors had a right to claim in view of the disclosure of the application that issued as the '940 patent. None of the patent claims is directed to a set comprising a first, second, and third DNA segment encoding a secretion signal operably linked to the heterologous fibrinogen Aα, Bβ and γ chains, respectively, each of the DNA segments comprising genomic DNA encoding the respective fibrinogen chain, and wherein each of the chains is from the same species and is operably linked to additional DNA segments required for expression in the mammary glands of a host female mammal. This set of DNA segments is useful in the methods of claims 1-20 and 23-25 of the '940 patent and in producing the non-human mammals of claims 21-22 and 26-33 of the '940 patent. I also believe that this set of DNA segments is described and enabled in the '940 patent. Finally, I believe that the set of DNA segments should have been claimed in the '940 patent and in the application from which it issued. Without a claim to this set of DNA segments, I understand and believe that a third party might potentially prepare the recited set of DNA segments in the United States and export that set from the United States for use outside the United States in the production of fibrinogen in the milk of transgenic animals. I also understand and believe that without reissue such acts would not infringe the claims of the '940 patent.

10. The error described in paragraph 11 arose without deceptive intent. Today, I do not recall the specific details of the prosecution of the patent application that issued as the '940 patent. Nonetheless, to the best of my recollection, I believe that I did not claim the set of DNA segments now claimed in reissue claim 34, because I was focusing on the end product -- fibrinogen -- and the methods and animals used to make it. I did not, as I recall, consider claiming the various intermediates -- including this set of DNA segments -- used in producing those animals or the claimed method.

11. I discovered these errors (paragraphs 4-7 and 8-10) in the claims of the '940 patent while reviewing the '940 patent, with counsel, in connection with Garner v. Velander, Interference 104,242.

12. I hereby declare that I understand the English language, and that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application for reissue or any Patent issued thereon.

Gary E. Parker

GARY E. PARKER

Date: Jan. 13, 1999

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Patentee	:	Ian Garner, Michael A.. Dalrymple,* Donna E. Prunkard and Donald C. Foster
Assignee	:	Pharmaceutical Proteins, Ltd., and ZymoGenetics, Inc.
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For	:	PRODUCTION OF FIBRINOGEN IN TRANSGENIC ANIMALS

Hon. Assistant Commissioner for Patents
Washington, D.C. 20231

CONSENT OF ASSIGNEE TO REISSUE APPLICATION

Sir:

ZymoGenetics, Inc., a co-assignee of the above-identified '940 patent, by virtue of an August 19, 1994 assignment of United States patent application 08/206,176, filed March 3, 1994, from Donna E. Prunkard and Donald C. Foster, recorded at Reel 7166, Frame 0921, hereby consents to the above-identified reissue of the '940 Patent.

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* The '940 patent incorrectly printed the middle initial of Dr. Dalrymple as "L."

EXPRESS MAIL
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Pursuant to 37 C.F.R. §§ 1.172 and 3.73(b), the undersigned hereby states and certifies that:

1. I am an officer of assignee corporation and am authorized to act on behalf of assignee corporation with respect to the above identified '940 Patent and this reissue thereof; and

2. The relevant evidentiary documents have been reviewed and, to the best of my knowledge and belief, an undivided share of the title to the '940 Patent is in the assignee.

ZYMOGENETICS, INC.,

Date ________

By: [signature]

Name: SHINKO Campos.

Title: Sr. V.P. Finance + Admin.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Hon. Assistant Commissioner for Patents
Washington, D.C. 20231

CONSENT OF ASSIGNEE TO REISSUE APPLICATION

Sir:

Pharmaceutical Proteins, Ltd., a co-assignee of the above-identified '940 Patent, by virtue of an August 12, 1994 assignment of United States patent application 08/206,176, filed March 3, 1994, from Ian Garner and Michael A. Dalrymple, recorded at Reel 7166, Frame 0931, hereby consents to the above-identified reissue of the '940 Patent.

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* The '940 patent incorrectly printed the middle initial of Dr. Dalrymple as "L".

EXPRESS MAIL
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Pursuant to 37 C.F.R. §§ 1.172 and 3.73(b), the undersigned hereby states and certifies that:

1. I am an officer of assignee corporation and am authorized to act on behalf of assignee corporation with respect to the above identified '940 Patent and this reissue thereof; and

2. The relevant evidentiary documents have been reviewed and, to the best of my knowledge and belief, an undivided share of the title to the '940 Patent is in the assignee.

PHARMACEUTICAL PROTEINS, LTD.

15/1/99
Date

By: Alan Colman

Name: ALAN COLMAN

Title: RESEARCH DIRECTOR